What we claim is:

1. A reagent composition which comprises an aqueous carrier and an admixture of at least two different terminators of a nucleic acid template-dependent, primer extension reaction, each of the terminators being capable of specifically terminating the extension reaction in a manner strictly dependent on the identity of the unpaired nucleotide base in the template immediately adjacent to, and downstream of, the 3' end of the primer, and at least one of the terminators being labeled with a detectable marker.

2. A reagent of claim 1, wherein the reagent comprises four different terminators.

3. A reagent of claim 2, wherein two of the terminators are labeled, each with a different detectable marker.

4. A reagent of claim 2, wherein three of the terminators are labeled, each with a different detectable marker.

5. A reagent of claim 2, wherein the four terminators are labeled, each with a different detectable marker.

6. A reagent of any of claims 1-5, wherein the terminator(s) comprise(s) a nucleotide or nucleotide analog.

7. A reagent of claim 6, wherein the terminator(s) comprise(s) dideoxynucleotides.

8. A reagent of claim 6, wherein the terminator(s) comprise(s) arabinoside triphosphates.

9. A reagent of claim 7, wherein the terminator(s) comprise(s) one or more of ddATP, ddCTP, ddGTP or ddTTP.

10. A reagent of any of claims 1-5, wherein each of the different detectable markers is an isotopically labeled moiety, a chromophore, a fluorophore, a protein moiety, or a moiety to which an isotopically labeled moiety, a chromophore, a fluorophore, or a protein moiety can be attached.

11. A reagent of claim 10, wherein each of the different detectable markers is a different fluorophore.

12. A reagent of any of claims 1-5, wherein the reagent further comprises pyrophosphatase.

13. A method of determining the identity of a nucleotide base at a specific position in a nucleic acid of interest which comprises:

(a) treating a sample containing the nucleic acid of interest, if such nucleic acid is double-stranded, so as to obtain unpaired nucleotide bases spanning the specific position, or directly employing step (b) if the nucleic acid of interest is single-stranded;

(b) contacting the sample from step (a), under hybridizing conditions, with an oligonucleotide primer which is capable of hybridizing with a stretch of nucleotide bases present in the nucleic acid of

interest, immediately adjacent to the nucleotide base to be identified, so as to form a duplex between the primer and the nucleic acid of interest such that the nucleotide base to be identified is the first unpaired base in the template immediately downstream of the 3′ end of the primer in said duplex;

(c) contacting the duplex from step (b) with a reagent of claim 5, under conditions permitting base pairing of a complementary terminator present in the reagent with the nucleotide base to be identified and occurrence of a template-dependent, primer extension reaction so as to incorporate the terminator at the 3′ end of the primer, the net result being that the primer has been extended by one terminator; and

(d) determining the identity of the detectable marker present at the 3′ end of the extended primer from step (c) and thereby determining the identity of the nucleotide base at the specific position in the nucleic acid of interest.

14. A method of determining the identity of a nucleotide base at a specific position in a nucleic acid of interest which comprises:

(a) treating a sample containing the nucleic acid of interest, if such nucleic acid is double-stranded, so as to obtain unpaired nucleotide bases spanning the specific position, or directly employing step (b)

if the nucleic acid of interest is single-stranded;

(b) contacting the sample from step (a), under hybridizing conditions, with an oligonucleotide primer which is capable of hybridizing with a stretch of nucleotide bases present in the nucleic acid of interest, immediately adjacent to the nucleotide base to be identified, so as to form a duplex between the primer and the nucleic acid of interest such that the nucleotide base to be identified is the first unpaired base in the template immediately downstream of the 3' end of the primer in said duplex;

(c) contacting the duplex from step (b) with a reagent of claim 2, wherein only one of the terminators has a detectable marker, under conditions permitting base pairing of a complementary terminator present in the reagent with the nucleotide base to be identified and occurrence of a template-dependent primer extension reaction so as to incorporate the terminator at the 3' end of the primer, the net result being that the primer has been extended by one terminator;

(d) repeating step (c) three additional times, with a different one of each of the four terminators being labeled in each of the four parallel reaction steps; and,

(e) determining which of the products of the four parallel template-dependent, primer

extension reactions has a detectable marker present at the 3' end of the primer and thereby determining the identity of the nucleotide base at the specific position in the nucleic acid of interest.

15. A method of determining the presence or absence of a particular nucleotide sequence in a sample of nucleic acids which comprises:

(a) treating the sample of nucleic acids, if such sample of nucleic acids contains double-stranded nucleic acids, so as to obtain single-stranded nucleic acids, or directly employing step (b) if the sample of nucleic acids contains only single-stranded nucleic acids;

(b) contacting the sample from step (a), under hybridizing conditions, with an oligonucleotide primer which is capable of hybridizing with the particular nucleotide sequence, if the particular nucleotide sequence is present, so as to form a duplex between the primer and the particular nucleotide sequence;

(c) contacting the duplex, if any, from step (b) with a reagent of claim 5, under conditions permitting base pairing of a complementary terminator present in the reagent with the unpaired template nucleotide base immediately downstream of the 3' end of the primer, the primer being hybridized with the particular nucleotide sequence in the template, and occurrence of a template-dependent, primer extension

reaction so as to incorporate the terminator at the 3' end of the primer; and,

(d) determining the absence or presence and identity of a detectable marker at the 3' end of the primer from step (c) and thereby determining the presence or absence of the particular nucleotide sequence in the sample of nucleic acids.

16. A method of determining the presence or absence of a particular nucleotide sequence in a sample of nucleic acids which comprises:

(a) treating the sample of nucleic acids, if such sample of nucleic acids contains double-stranded nucleic acids, so as to obtain single-stranded nucleic acids, or directly employing step (b) if the sample of nucleic acids contains only single-stranded nucleic acids;

(b) contacting the sample from step (a), under hybridizing conditions, with an oligonucleotide primer which is capable of hybridizing with the particular nucleotide sequence, if the particular nucleotide sequence is present, so as to form a duplex between the primer and the particular nucleotide sequence;

(c) contacting the duplex, if any, from step (b) with a reagent of claim 2, wherein only one of the terminators has a detectable marker, under conditions permitting base pairing of a complementary

terminator present in the reagent with the unpaired template nucleotide base immediately downstream of the 3' end of the primer, the primer being hybridized with the particular nucleotide sequence in the template, and occurrence of a template-dependent, primer extension reaction so as to incorporate the terminator at the 3' end of the primer;

(d) repeating step (c) three additional times, with a different one of each of the four terminators being labeled in each of the four parallel reaction steps; and,

(e) determining the absence or presence and identity of a detectable marker at the 3' end of the primer in the products of each of the four parallel template-dependent, primer extension reactions and thereby determining the presence or absence of the particular nucleotide sequence in the sample of nucleic acids.

17. A method of typing a sample containing nucleic acids which comprises identifying the nucleotide base or bases present at each of one or more specific positions, each such nucleotide base being identified using the method of claim 13 or 14, and each such specific position being determined using a different primer.

18. A method of claim 17, wherein the identity of each nucleotide base or bases at each position is determined individually or wherein the identities of the nucleotide bases at different positions are determined simultaneously.

19. A method of typing a sample containing nucleic acids which comprises determining the presence or absence of one or more particular nucleotide sequences, the presence or absence of each such nucleotide sequence being determined by the method of claim 15 or 16.

20. A method of typing a sample containing nucleic acids which comprises:

(a) determining the presence or absence of one or more particular nucleotide sequences, the presence or absence of each such nucleotide sequence being determined by the method of claim 15 or 16; and,

(b) identifying the nucleotide base or bases present at each of one or more specific positions, each such nucleotide base being identified using the method of claim 13 or 14, and each such specific position being determined using a different primer.

21. A method for identifying different alleles in a sample containing nucleic acids which comprises identifying the nucleotide base or bases present at each of one or more specific positions, each such nucleotide base being identified by the method of claim 13 or 14.

22. A method for determining the genotype of an organism at one or more particular genetic loci which comprises:

(a) obtaining from the organism a sample containing genomic DNA; and

(b) identifying the nucleotide base or bases present at each of one or more specific positions in nucleic acids of interest, each such base or bases being identified using the method of claim 13 or 14, and thereby identifying different alleles and thereby, in turn, determining the genotype of the organism at one or more particular genetic loci.

23. A method of claim 13 or 14, wherein the conditions for the occurrence of the template-dependent, primer extension reaction in step (c) are created, in part, by the presence of a suitable template-dependent enzyme.

24. A method of claim 23, wherein the template-dependent enzyme is E. coli DNA polymerase I or the "Klenow fragment" thereof, T4 DNA polymerase, T7 DNA polymerase ("Sequenase"), T. aquaticus DNA polymerase, a retroviral reverse transcriptase, or combinations thereof.

25. A method of claim 13 or 14, wherein the nucleic acid of interest is a deoxyribonucleic acid, a ribonucleic acid, or a copolymer of deoxyribonucleic acid and ribonucleic acid.

26. A method of claim 13 or 14, wherein the primer is an oligodeoxyribonucleotide, an oligoribonucleotide, or a copolymer of deoxyribonucleic acid and ribonucleic acid.

27. A method of claim 13 or 14, wherein the template is a deoxyribonucleic acid, the primer is an oligodeoxyribonucleotide, oligoribonucleotide, or a copolymer of deoxyribonucleotides and

ribonucleotides, and the template-dependent enzyme is a DNA polymerase.

28. A method of claim 13 or 14, wherein the template is a ribonucleic acid, the primer is an oligodeoxyribonucleotide, oligoribonucleotide, or a copolymer of deoxyribonucleotides and ribonucleotides, and the template-dependent enzyme is a reverse transcriptase.

29. A method of claim 13 or 14, wherein the template is a deoxyribonucleic acid, the primer is an oligoribonucleotide, and the enzyme is an RNA polymerase.

30. A method of claim 13 or 14, wherein the template is a ribonucleic acid, the primer is an oligoribonucleotide, and the template-dependent enzyme is an RNA replicase.

31. A method of claim 13 or 14, wherein, prior to the primer extension reaction in step (c), the template has been capped at its 3' end by the addition of a terminator to the 3' end of the template, said terminator being capable of terminating a template-dependent, primer extension reaction.

32. A method of claim 31, wherein the terminator is a dideoxynucleotide.

33. A method of claim 13 or 14, wherein the nucleic acid of interest has been synthesized enzymatically in vivo, synthesized enzymatically in vitro, or synthesized non-enzymatically.

34. A method of claim 13 or 14, wherein the oligonucleotide primer has been synthesized

enzymatically in vivo, synthesized enzymatically in vitro, or synthesized non-enzymatically.

35. A method of claim 13 or 14, wherein the oligonucleotide primer comprises one or more moieties that permit affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest.

36. A method of claim 35, wherein the oligonucleotide primer comprises biotin which permits affinity separation of the primer from the unincorporated reagent and/or nucleic acid of interest via binding of the biotin to streptavidin which is attached to a solid support.

37. A method of claim 13 or 14, wherein the sequence of the oligonucleotide primer comprises a DNA sequence that permits affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest via base pairing to a complementary sequence present in a nucleic acid attached to a solid support.

38. A method of claim 13 or 14, wherein the nucleic acid of interest comprises one or more moieties that permit affinity separation of the nucleic acid of interest from the unincorporated reagent and/or the primer.

39. A method of claim 38, wherein the nucleic acid of interest comprises biotin which permits affinity separation of the nucleic acid of interest from the unincorporated reagent and/or the primer via binding of the biotin to streptavidin which is attached to a solid support.

40. A method of claim 13 or 14, wherein the sequence of the nucleic acid of interest comprises a DNA sequence that permits affinity separation of the nucleic acid of interest from the unincorporated reagent and/or the primer via base pairing to a complementary sequence present in a nucleic acid attached to a solid support.

41. A method of claim 13 or 14, wherein the oligonucleotide primer is labeled with a detectable marker.

42. A method of claim 41, wherein the oligonucleotide primer is labeled with a detectable marker that is different from any detectable marker present in the reagent or attached to the nucleic acid of interest.

43. A method of claim 13 or 14, wherein the nucleic acid of interest is labeled with a detectable marker.

44. A method of claim 43, wherein the nucleic acid of interest is labeled with a detectable marker that is different from any detectable marker present in the reagent or attached to the primer.

45. A method of claim 13 or 14, wherein the nucleic acid of interest comprises non-natural nucleotide analogs.

46. A method of claim 45, wherein the non-natural nucleotide analogs comprise deoxyinosine or 7-deaza-2'-deoxyguanosine.

47. A method of claim 13 or 14, wherein the nucleic acid of interest has been synthesized by the polymerase chain reaction.

48. A method of claim 13 or 14, wherein the sample comprises genomic DNA from an organism, RNA transcripts thereof, or cDNA prepared from RNA transcripts thereof.

49. A method of claim 13 or 14, wherein the sample comprises extragenomic DNA from an organism, RNA transcripts thereof, or cDNA prepared from RNA transcripts thereof.

50. A method of claim 13 or 14, wherein the primer is substantially complementary to the known base sequence immediately adjacent to the base to be identified.

51. A method of claim 13 or 14, wherein the primer is fully complementary to the known base sequence immediately adjacent to the base to be identified.

52. A method of claim 13 or 14, wherein the primer is separated from the nucleic acid of interest after the primer extension reaction in step (c) by using appropriate denaturing conditions.

53. A method of claim 52, wherein the denaturing conditions comprise heat, alkali, formamide, urea, glyoxal, enzymes, and combinations thereof.

54. A method of claim 53, wherein the denaturing conditions comprise treatment with 0.2 N NaOH.

55. A method of claim 48, wherein the organism is a plant, microorganism, virus, or bird.

56. A method of claim 48, wherein the organism is a vertebrate or invertebrate.

57. A method of claim 48, wherein the organism is a mammal.

58. A method of claim 57, wherein the mammal is a human being.

59. A method of claim 57, wherein the mammal is a horse, dog, cow, cat, pig, or sheep.

Add C1